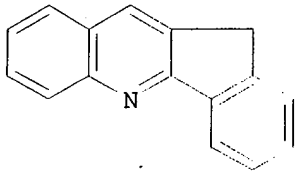

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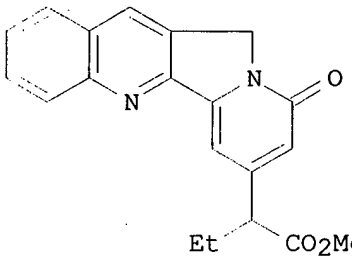

II

AB Photolysis of N-propargyl-6-halo-2-pyridones and related arom. halides in the presence of aryl isonitriles provides tetra- and penta-cyclic products, e.g. I and II, in a single step by a sequence of radical addn. to the isonitrile followed by two cyclizations. The scope and limitations of the process are described along with a first generation synthesis of racemic camptothecin.

=> fil caol;s l3

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1957-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

L4 0 L3

=> del his y

BERCH
921102

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=> fil reg

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USE IS SUBJECT TO THE TERMS OF YOUR . IN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES:  27 APR  98  HIGHEST RN 204632-65-5
DICTIONARY FILE UPDATES: 27 APR  98  HIGHEST RN 204594-19-4

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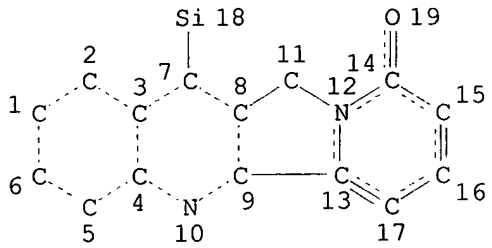

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L3 ANSWER 1 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203923-85-7 REGISTRY
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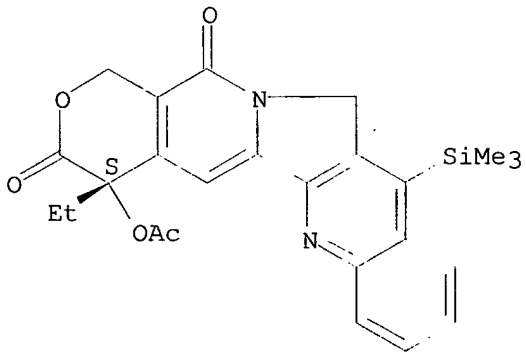
OTHER NAMES:
CN 20-O-Acetyl-7-trimethylsilylcamptothecin
FS STEREOSEARCH
MF C25 H26 N2 O5 Si
SR CA
LC STN Files: CA, CAPLUS

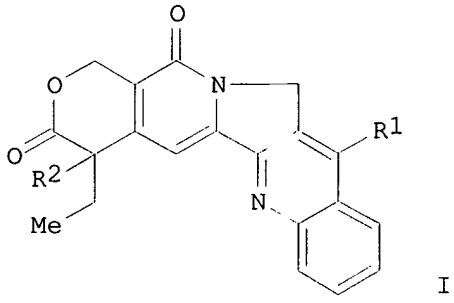
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:205022 synthesis of highly lipophilic camptothecin derivatives. Hausheer, Frederick Herman; Haridas, Kochat; Seetharamulu, Peddaiahgari; Murali, Dhanabalan; Reddy, Dasharatha Gauravaram; Yao, Shijie; Petluru, Pavankumar (Bionumerik Pharmaceuticals, Inc., USA; Lucas, Brian Ronald; Hausheer, Frederick Herman; Haridas, Kochat; Seetharamulu, Peddaiahgari; Murali, Dhanabalan; Reddy, Dasharatha Gauravaram; Yao, Shijie; Petluru, Pavankumar). PCT Int. Appl. WO 9807727 A1 980226, 58 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 97-GB2205 970815. PRIORITY: US 96-24171 960819.

GI

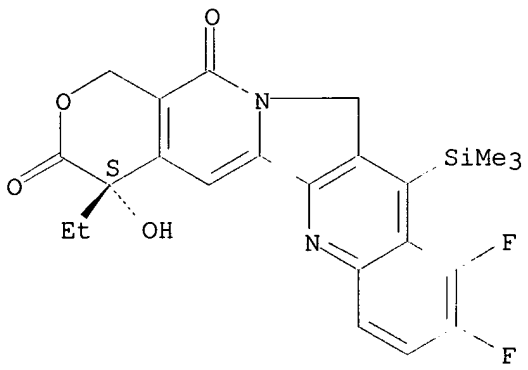


I

AB Lipophilic camptothecin derivs. (I) [R1 = C(O)R3, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted aryl, SR4, halo, oxo, S(O)R5, OSO2CF3, substituted silyl; R2 = H, OH, protected OH; R3 = (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted, halo; R4 = R5 = (un)substituted alkyl] were prepd. in the form of the free bases or pharmaceutically acceptable acid addn. salts as highly lipophilic, lactone stable, and do not require metabolic activation, and are anti-neoplastic compds.

L3 ANSWER 2 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-83-5 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-9,10-difluoro-4-hydroxy-11-(trimethylsilyl)-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H22 F2 N2 O4 Si
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

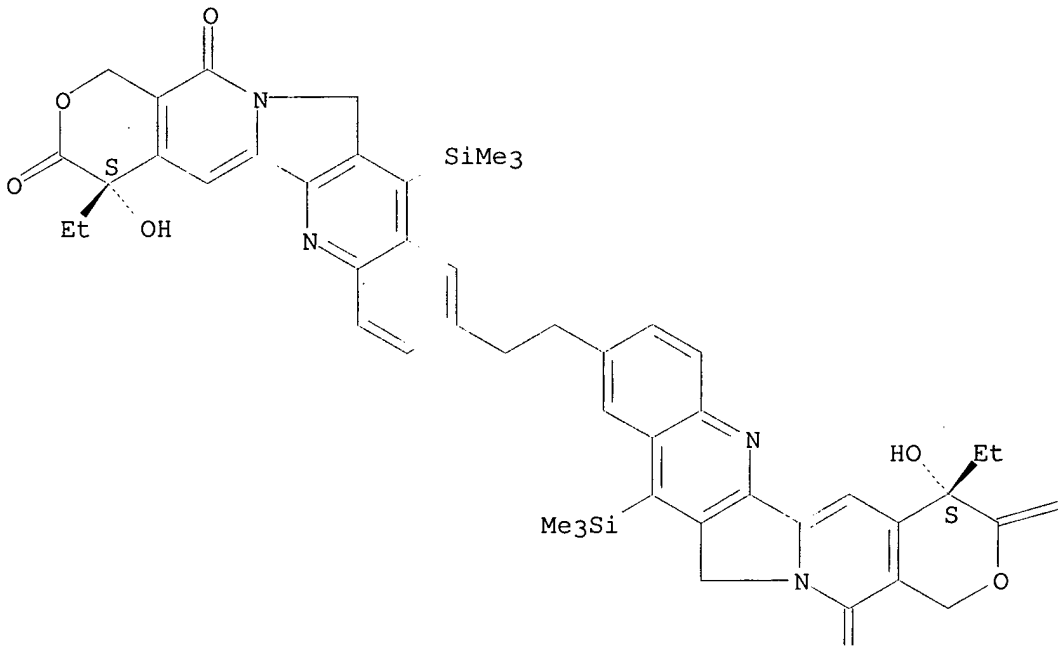
REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 3 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-82-4 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 9,9'-(1,2-ethanediyl)bis[4-ethyl-4-hydroxy-11-(trimethylsilyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C48 H50 N4 O8 Si2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

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PAGE 2-A

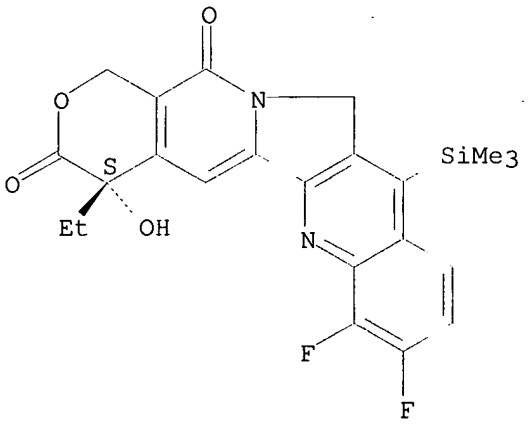
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 4 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-81-3 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-7,8-difluoro-4-hydroxy-11-(trimethylsilyl)-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H22 F2 N2 O4 Si
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

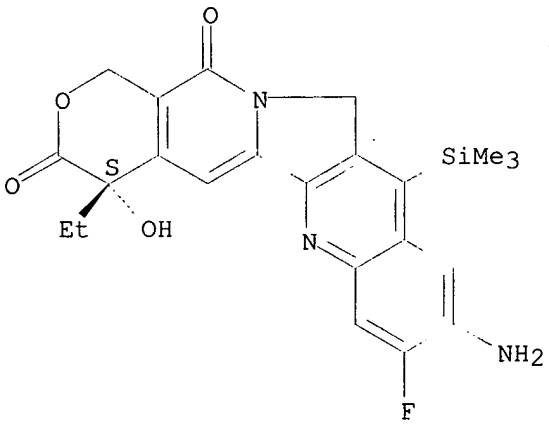
REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 5 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-80-2 REGISTRY

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 9-amino-4-ethyl-8-fluoro-4-hydroxy-11-(trimethylsilyl)-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H24 F N3 O4 Si
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..
AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 6 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-79-9 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-8-fluoro-4-hydroxy-11-(trimethylsilyl)-, (S)- (9CI) (CA INDEX NAME)
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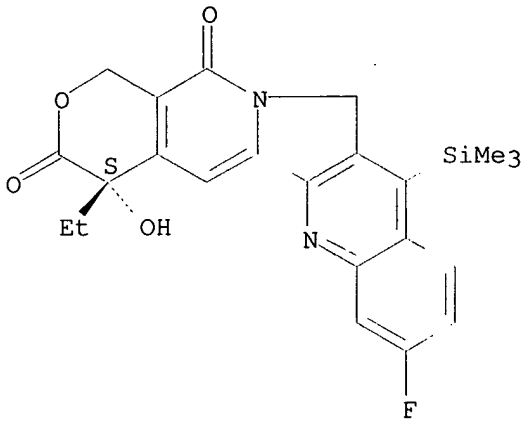
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 7 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-78-8 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-10-fluoro-4-hydroxy-11-(trimethylsilyl)-, (S)- (9CI) (CA INDEX NAME)
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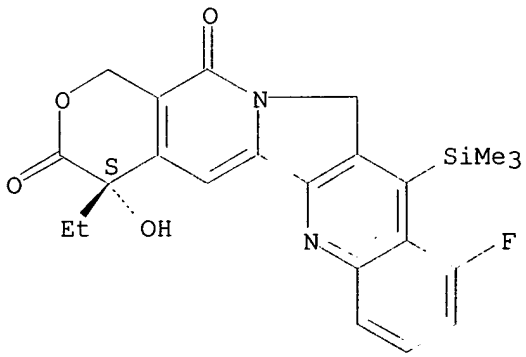
MF C23 H23 F N2 O4 Si
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 8 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-77-7 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 8-amino-4-ethyl-4-hydroxy-11-(trimethylsilyl)-, (S)- (9CI) (CA INDEX NAME)
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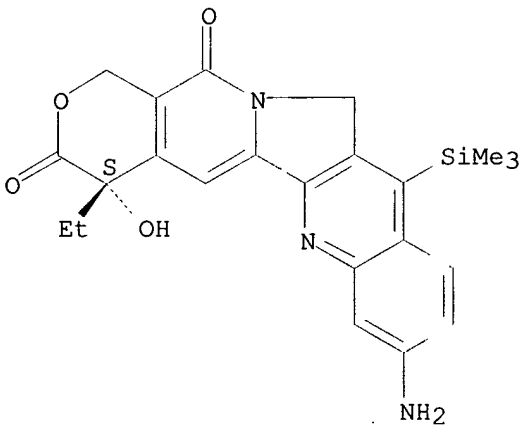
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 9 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-76-6 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 9-amino-4-ethyl-4-hydroxy-11-(trimethylsilyl)-, (S)- (9CI) (CA INDEX NAME)
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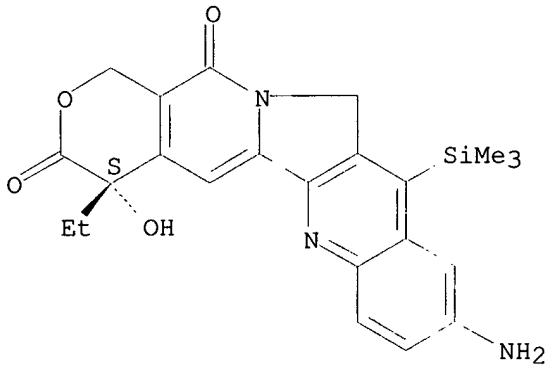
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 10 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-75-5 REGISTRY
CN Indolizino[1,2-b]quinoline-7-acetamide, N-[2-(dimethylamino)ethyl]-.alpha.-ethyl-9,11-dihydro-.alpha.,2-dihydroxy-9-oxo-8-[(1-oxopropoxy)methyl]-12-(trimethylsilyl)-, (S)- (9CI) (CA INDEX NAME)
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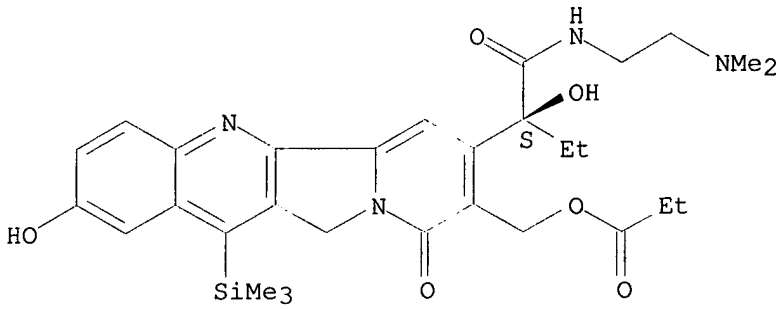
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



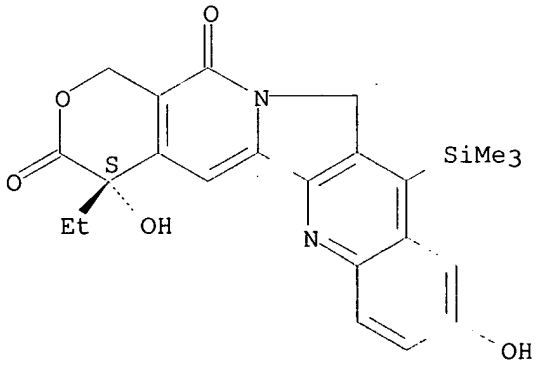
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 11 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-74-4 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-4,9-dihydroxy-11-(trimethylsilyl)-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H24 N2 O5 Si
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

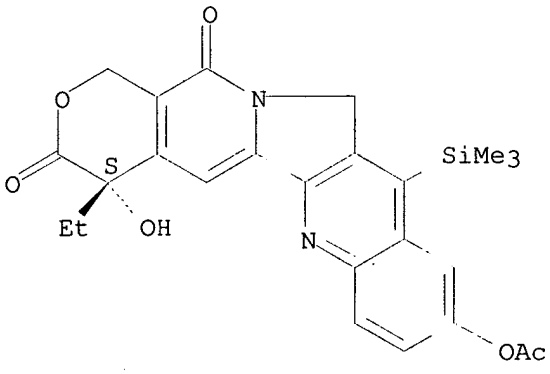
REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new

family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 12 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-73-3 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 9-(acetyloxy)-4-ethyl-4-hydroxy-11-(trimethylsilyl)-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H26 N2 O6 Si
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

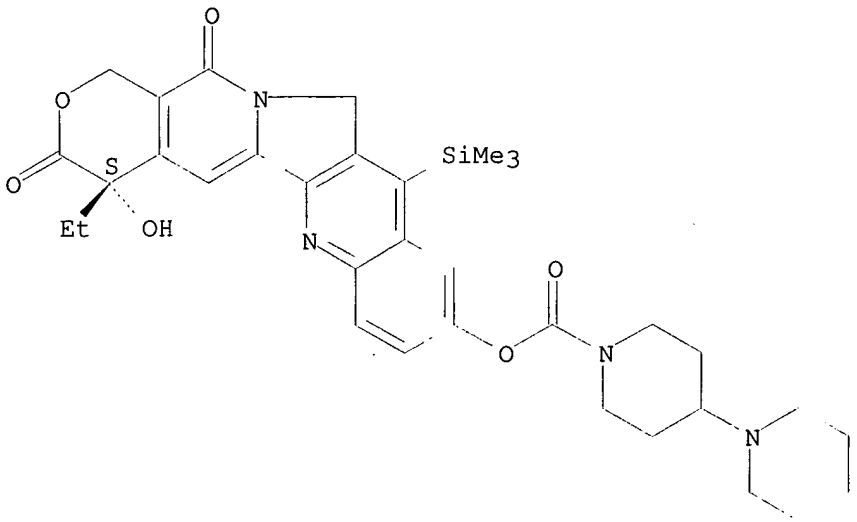
REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 13 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-72-2 REGISTRY
CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4-ethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-11-(trimethylsilyl)-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, (S)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH
MF C34 H42 N4 O6 Si
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



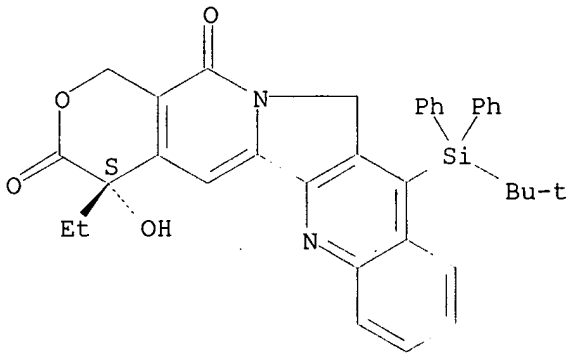
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 14 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-71-1 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 11-[(1,1-dimethylethyl)diphenylsilyl]-4-ethyl-4-hydroxy-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H34 N2 O4 Si
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



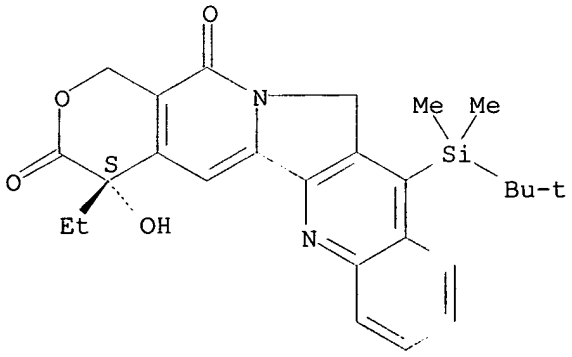
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 15 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-70-0 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 11-[(1,1-dimethylethyl)dimethylsilyl]-4-ethyl-4-hydroxy-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H30 N2 O4 Si
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



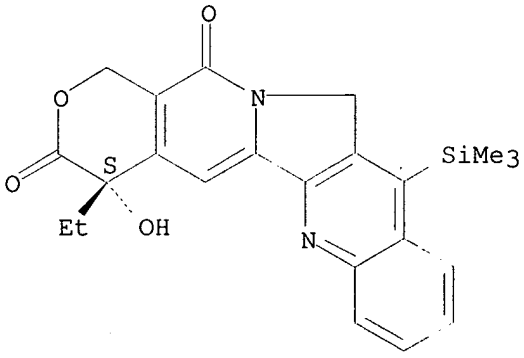
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 16 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 203173-69-7 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-4-hydroxy-11-(trimethylsilyl)-, (S)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 7-Trimethylsilylcamptothecin
FS STEREOSEARCH
MF C23 H24 N2 O4 Si
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:205022 synthesis of highly lipophilic camptothecin derivatives. Hausheer, Frederick Herman; Haridas, Kochat; Seetharamulu, Peddaiahgari; Murali, Dhanabalan; Reddy, Dasharatha Gauravaram; Yao, Shijie; Petluru, Pavankumar (Bionumerik Pharmaceuticals, Inc., USA; Lucas, Brian Ronald; Hausheer, Frederick Herman; Haridas, Kochat; Seetharamulu, Peddaiahgari; Murali, Dhanabalan; Reddy, Dasharatha Gauravaram; Yao, Shijie; Petluru, Pavankumar). PCT Int. Appl. WO 9807727 A1 980226, 58 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 97-GB2205 970815. PRIORITY: US 96-24171

960819.

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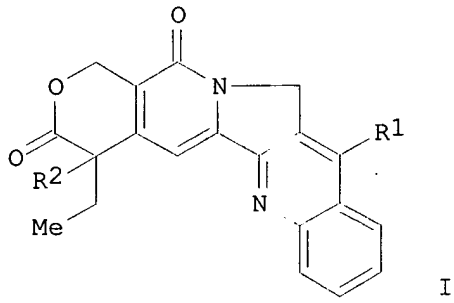


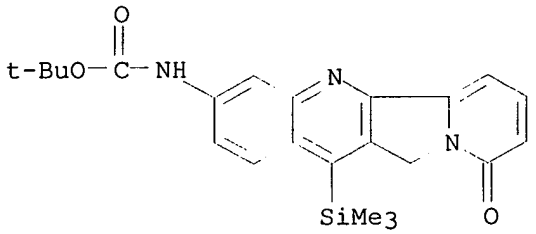
I

AB Lipophilic camptothecin derivs. (I) [R1 = C(O)R3, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted aryl, SR4, halo, oxo, S(O)R5, OSO2CF3, substituted silyl; R2 = H, OH, protected OH; R3 = (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted, halo; R4 = R5 = (un)substituted alkyl] were prepd. in the form of the free bases or pharmaceutically acceptable acid addn. salts as highly lipophilic, lactone stable, and do not require metabolic activation, and are anti-neoplastic compds.

REFERENCE 2: 128:175876 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents. Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Bioorg. Med. Chem. Lett., 7(24), 3189-3194 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compd., 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

L3 ANSWER 17 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 202745-22-0 REGISTRY
CN Carbamic acid, [9,11-dihydro-9-oxo-12-(trimethylsilyl)indolizino[1,2-b]quinolin-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H27 N3 O3 Si
SR CA
LC STN Files: CA, CAPLUS

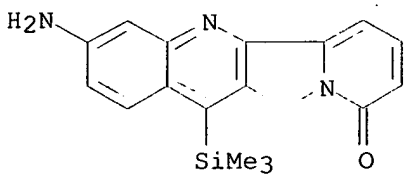


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:154267 A general synthetic approach to the (20S)-camptothecin family of antitumor agents by a regiocontrolled cascade radical cyclization of aryl isonitriles. Josien, Hubert; Ko, Sung-Bo; Bom, David; Curran, Dennis P. (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Chem.--Eur. J., 4(1), 67-83 (English) 1998. CODEN: CEUJED. ISSN: 0947-6539. Publisher: Wiley-VCH Verlag GmbH.

AB A general and efficient synthesis of (20S)-camptothecin (I) was reported. A key common intermediate contg. the pyridone and lactone (DE) rings of camptothecin and most derivs. was constructed from 2-trimethylsilyl-6-methoxypyridine by a series of metalation reactions and a Heck cyclization to provide an achiral bicyclic enol ether. Sharpless asym. dihydroxylation followed by lactol oxidn. and iododesilylation produced the key intermediate in 94% enantiomeric excess. Alkylation with propargyl bromide and a cascade radical reaction with PhNC then produced I. About 20 other penta- and hexacyclic analogs of camptothecin with differing single or multiple substituents at C7, C9, C10, C11, and/or C12 were made by changing the propargylating agent and the isonitrile. Included among these are several drug candidates and the approved drugs topotecan and irinotecan. The synthesis of the prodrug irinotecan is a direct one that does not pass through the active metabolite. The use of ortho-trimethylsilyl-substituted isonitriles allows the regioselective synthesis of camptothecin analogs in cases where isomeric mixts. are formed from the parent isonitriles. The synthesis of the derivs. relies on the broad scope and functional group tolerance of the key cascade radical reaction.

L3 ANSWER 18 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 202745-02-6 REGISTRY
CN Indolizino[1,2-b]quinolin-9(11H)-one, 3-amino-12-(trimethylsilyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H19 N3 O Si
SR CA
LC STN Files: CA, CAPLUS



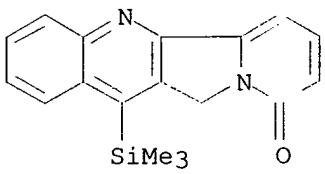
1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:154267 A general synthetic approach to the (20S)-camptothecin family of antitumor agents by a regiocontrolled cascade radical cyclization of aryl isonitriles. Josien, Hubert; Ko, Sung-Bo; Bom, David; Curran, Dennis P. (Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA). Chem.--Eur. J., 4(1), 67-83 (English) 1998. CODEN: CEUJED. ISSN: 0947-6539. Publisher: Wiley-VCH Verlag GmbH.

AB A general and efficient synthesis of (20S)-camptothecin (I) was reported. A key common intermediate contg. the pyridone and lactone (DE) rings of camptothecin and most derivs. was constructed from 2-trimethylsilyl-6-methoxypyridine by a series of metalation reactions and a Heck cyclization to provide an achiral bicyclic enol ether. Sharpless asym. dihydroxylation followed by lactol oxidn. and iododesilylation produced the key intermediate in 94% enantiomeric excess. Alkylation with propargyl bromide and a cascade radical reaction with PhNC then produced I. About 20 other penta- and hexacyclic analogs of camptothecin with differing single or multiple substituents at C7, C9, C10, C11, and/or C12 were made by changing the propargylating agent and the isonitrile. Included among these are several drug candidates and the approved drugs topotecan and irinotecan. The synthesis of the prodrug irinotecan is a direct one that does not pass through the active metabolite. The use of ortho-trimethylsilyl-substituted isonitriles allows the regioselective synthesis of camptothecin analogs in cases where isomeric mixts. are formed from the parent isonitriles. The synthesis of the derivs. relies on the broad scope and functional group tolerance of the key cascade radical reaction.

L3 ANSWER 19 OF 19 REGISTRY COPYRIGHT 1998 ACS
RN 182276-00-2 REGISTRY
CN Indolizino[1,2-b]quinolin-9(11H)-one, 12-(trimethylsilyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H18 N2 O Si
SR CA
LC STN Files: CA, CAPLUS



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:276262 Tandem radical reactions of isonitriles with 2-pyridonyl and other aryl radicals: scope and limitations, and a first generation synthesis of (.+-.)-camptothecin. Curran, Dennis P.; Liu, Hui; Josien, Hubert; Ko, Sung-Bo (Dep. Chem., Univ. Pittsburgh, Pittsburgh, PA, 15260, USA). Tetrahedron, 52(35), 11385-11404 (English) 1996. CODEN: TETRAB. ISSN: 0040-4020.

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